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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,727	GAU, VINCENT JEN-JR.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *83-95,98-104,108,112-118,120-127,129 and 130* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83-95,98-104,108,112-118,120-127,129 and 130* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

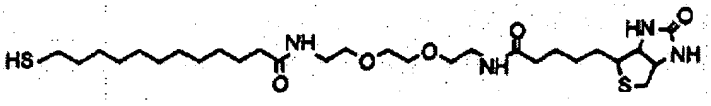
DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 07/03/2006 are acknowledged and entered.

2. Claims 83-95, 98-104, 108, 112-118, and 120-130 were pending. Applicants have amended claims 83 and 123; and cancelled claim 128. No claims were added. Therefore, claims 83-95, 98-104, 108, 112-118, 120-122, 124-127, and 129-130 are currently pending, and are under consideration in this Office Action.

Withdrawn Rejection(s) and Indication of Allowable Subject Matter

3. All previous 103 rejections are withdrawn in view of applicants' amendments of claims 83 and 123, and cancellation of claim 128. The amendment of claim 83 included the addition of the limitation of claim 128 that is "*the molecules are biotinylated thiols*" into claim 83 for the reason that claim 128 was indicated as being allowable. However, the indicated allowability of Claim 128 is withdrawn upon reconsideration of the its claimed limitation, i.e. "*the molecules are biotinylated thiols*", in view of Spinkle et al. (*Langmuir*, **1993**, 9(7), pgs. 1821-1825). Spinkle et al. disclose a "*biotinylated thiol*" molecule that is 12-mercapto(8-biotinamide-3,6-dioxaoctyl)dodecanamide (i.e. ). This is also applicant exemplify species of a "*biotinylated thiol*" molecule (i.e. biotin-DAD-C12-SH) as indicated in the response filed 07/03/2006; see pg. 8, last paragraph. Accordingly, this Office Action is a Non-Final Office Action and the examiner apologizes for any inconvenience.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 83, 126, 127, and 130 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The independent claim 83 is amended to specify a '*self-assembly monolayer including biotinylated thiol molecules that include a sulfur that is bonded directly to at least one electrode selected from a group consisting of a working electrode, the reference electrode, and the counter electrode*', i.e. the biotinylated thiol self-assembly monolayer is bonded to an electrode wherein the electrode can be "*a working electrode, the reference electrode, and the counter electrode*".

Claims 126 and 127 recite that the biotinylated thiol self-assembly monolayer is positioned on the working electrode, the reference electrode, and the counter electrode, i.e. the biotinylated thiol self-assembly monolayer is bonded on all three electrodes. Claim 130 recites that the self-assembly monolayer is positioned on the reference electrode, i.e. the biotinylated thiol self-assembly monolayer is bonded on the reference electrode.

The specification as originally filed provided no implicit or explicit support for the limitations that biotinylated thiol self-assembly monolayer is bonded a) on a 'single' counter electrode as claimed in claim 83; b) on all three electrodes, i.e. the working electrode, the

reference electrode, and the counter electrode as claimed in claims 126 and 127; and c) on a 'single' reference electrode as claimed in claims 83 and 130. The instant specification disclosed that the surface of the working electrode is modify using self-assembly monolayer for anchoring macromolecules (page 10, paragraph [064]) and specifically the sulfur containing self-assembly monolayer, i.e. biotinylated thiol self-assembly monolayer, is use to modify gold working electrode (page 30, paragraph [0139], lines 6-8), i.e. the biotinylated thiol self-assembly monolayer is bonded to working electrode. Accordingly, the instant specification has only provided support for the limitation that the biotinylated thiol self-assembly monolayer is bonded only on working electrode.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), and the MPEP 714.02, 3rd paragraph, last sentence. MPEP § 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP § 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application". MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved.

Applicant should therefore specifically point out the support for any amendments made to the disclosure.

Response to Arguments

6. Applicant's arguments directed to the 35 U.S.C. 112, first paragraph, new matter rejection were considered but they are not persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicant's newly amended and/or added claims and/or arguments.

[1] Applicant contends that the support for the amended claim 83 is found in paragraph [064], paragraph [0166], figure 20, and paragraph [0124].

[2] Applicant alleges that the support for claims 126 and 127 is found in paragraph [0166] and figure 20.

[3] Applicant argues that the support for claim 130 is found in figure 20.

This is not found persuasive for the following reasons:

[1] The examiner respectfully disagrees. It is the examiner's position that the disclosures of paragraph [064], paragraph [0166], figure 20, and paragraph [0124] do not support the amended claim 83. The amended claim 83 specify that '*self-assembly monolayer including biotinylated thiol molecules that include a sulfur that is bonded directly to at least one electrode selected from a group consisting of a working electrode, the reference electrode, and the counter electrode*', which can be reasonably interpreted that the biotinylated thiol self-assembly monolayer is bonded to 1) a 'single' specific electrode such as a working electrode, a reference electrode, or a counter electrode, or 2) any combination of electrodes such as a working electrode

and a reference electrode, a working electrode and a counter electrode, or a working electrode, a reference electrode, and a counter electrode. Paragraph [064] of page 10 (lines 5-6) provided that '*the SAM is placed on the surface of a working electrode in an electrochemical sensor*', i.e. the biotinylated thiol self-assembly monolayer is bonded to the working electrode, and as a result, provide only support for the biotinylated thiol self-assembly monolayer is bonded to the working electrode and ***not*** for the biotinylated thiol self-assembly monolayer is bonded to a reference electrode or a counter electrode. Paragraph [0166] of pages 40-41 disclose the experiment regarding the binding of streptavidin to the biotin SAM and bare Au (gold), which refers to figures 41. Moreover, figure 20 illustrate the biotinylated thiol self-assembly monolayer is bonded to a gold surface (ref. #680) and does not specifically illustrate the specific electrodes, i.e. the working electrode, the reference electrode, and the counter electrode. Additionally, paragraph [0124] of page 26 does not refer to figure 20, but rather to fig. 25.

Therefore, amended claim 83 has found no support in the originally filed specification, especially for the biotinylated thiol self-assembly monolayer that is bonded to 1) a 'single' specific electrode such as a reference electrode or a counter electrode, or 2) any combination of electrodes such as a working electrode and a reference electrode, a working electrode and a counter electrode, or a working electrode, a reference electrode, and a counter electrode.

[2] The examiner respectfully disagrees. It is the examiner's position that the disclosures of paragraph [0166] and figure 20 do not support the limitation of claims 126 and 127 wherein the biotinylated thiol self-assembly monolayer is bonded on all three electrodes on the working electrode, the reference electrode, and the counter electrode, i.e. the biotinylated thiol self-assembly monolayer. Paragraph [0166] of pages 40-41 disclose the experiment regarding the

binding of streptavidin to the biotin SAM and bare Au (gold), which refers to figures 41. Moreover, figure 20 illustrate the biotinylated thiol self-assembly monolayer is bonded to a gold surface (ref. #680) and does not specifically illustrate the specific electrodes, i.e. the working electrode, the reference electrode, and the counter electrode. Accordingly, the limitation of claims 126 and 127 has found no support in the originally filed specification wherein the biotinylated thiol self-assembly monolayer is bonded on all three electrodes.

[3] The examiner respectfully disagrees. It is the examiner's position that the disclosure of figure 20 do not support the limitation of claim 130 wherein the biotinylated thiol self-assembly monolayer is bonded on the reference electrode. Figure 20 illustrate the biotinylated thiol self-assembly monolayer is bonded to a gold surface (ref. #680) and does not specifically illustrate the specific electrodes, i.e. the working electrode, the reference electrode, and the counter electrode. Accordingly, the limitation of claim 130 has found no support in the originally filed specification wherein the biotinylated thiol self-assembly monolayer is bonded on the reference electrode.

Therefore, the originally filed specification has no support for the limitations of the amended claim 83, claims 126 and 127, and claim 130, and the rejection is maintained.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 129 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 129 recites the limitation "the molecules" in line. There is insufficient antecedent basis for this limitation in the claim 83 since the limitation of "molecules" of claim 83 has been deleted by the amendment filed 07/03/2006.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Spinkle et al. (*Langmuir*, **1993**, 9(7), pgs. 1821-1825) and Wink et al. (*The Analyst*, **1997**, 122(4), pgs. 43R-50R).

For ***claims 83, 98-101, 108, 112, 118, and 123***, Choong et al. disclose an apparatus and methods for electronic detection of single base extension following hybridization of a biological sample that reads on the presently claimed invention (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22).

The method comprises the steps of a) contacting the sample to the plurality of first electrodes (refers to the instant claimed positioning step), b) adding the reagent comprising the electrochemical redox labels that participates in the redox reaction at the surface of the electrode, c) detecting the electrical signal to identify the base extension wherein the detection step includes controlling the current flow between two electrodes (refers to the instant claimed conducting and employing steps and instant claims 108 and 123)(see e.g. col. 4, lines 39-53; col. 7, lines 41-50; col. 8, lines 9-35; col. 10, lines 10-41; col. 10, lines 15-30). In addition, Choong et al. disclose the step of forming the polymer onto the working electrode (see e.g. col. 11, lines 31-40).

The apparatus (refers to the instant claimed sensor) comprises a supporting substrate, a plurality of first electrode (refers to instant claimed working electrode), a counter electrode, and a reference electrode wherein the first electrode is in contact with a supporting substrate (refers to the instant claims 99 and 112) and oligonucleotide probes are immobilized on the first electrode via a polymer (refers to the instant claim 98)(see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The reference electrode comprises materials such as silver wire (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*" and the instant claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source (refers to instant claim 100)(see e.g. col. 7, lines 41-50).

For ***claims 85, 86, and 103***, Choong et al. disclose the sample comprise a solution of target nucleic acids (see e.g. col. 8, lines 9-13; col. 11, line 62 thru col. 12, line 4).

For ***claims 87 and 88***, Choong et al. teach that the substrate's material include materials such as silicon, glass, plastic, and ceramic (see e.g. col. 5, lines 54-58).

For ***claims 89, 90, 94, 101, and 118***, Choong et al. teach that the first electrode comprises materials such as gold, titanium, and platinum (see e.g. col. 5, line 59 thru col. 6, line 3). Choong et al. further teach that the counter electrode comprises materials such as gold, titanium, and platinum (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40).

For ***claim 113***, Choong et al. teach that the substrate has a surface area of between 0.01 μm^2 and 5 cm^2 (see e.g. col. 6, lines 12-26).

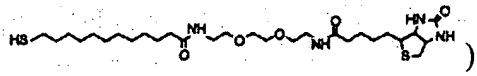
For ***claims 114-117***, Choong et al. further disclose that the detection methodology includes amperometric and cyclic voltammetry (refers to the instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41).

The teachings of Choong et al. differs from the presently claimed invention as follows:

For ***claims 83, 120, 124, 125 and 129***, Choong et al. fail to disclose a self-assembled monolayer on at least one electrode. More specifically, they do not teach that the self-assembled monolayer includes biotinylated thiol in which the sulfur is bonded directly onto the working electrode. Choong et al. further fail to disclose that each molecules of the self-assembled monolayer have the same molecular structure.

However, Spinkle et al. and Wink et al. teach the limitations that are deficient in Choong et al.

For ***claims 83, 120, 124, 125 and 129***, Spinkle et al. disclose a thiol monolayer and the method of making thiol monolayer onto a gold metal surface (see e.g. Abstract; pg. 1821, left

col., lines 29-33; pg. 1822, left col., lines 5-16). The thiol monolayer is a biotinylated thiol self-assembled monolayer, which is 12-mercapto(8-biotinamide-3,6-dioxaoctyl)dodecanamide (i.e. ). Although the self-assembled monolayer on the gold metal surface of Spinkle et al. is use in surface plasmon resonance, Wink et al. teach that a surface modified with sulfur containing self-assembled monolayer is employed in application such as electrochemical and surface plasmon resonance (Wink: pg. 45R, right col., line 1 thru pg. 48R, left col., line 2). Thus, any a surface modified with sulfur containing self-assembled monolayer use for surface plasmon resonance sensor can also be use for electrochemical sensor. Furthermore, the instant specification on page 24, paragraph [0116], recite using the procedure of Spinkle et al. for depositing biotin-DAD-C12-SH (12-mercapto(8-biotinamide-3,6-dioxaoctyl)dodecanamide) onto an Au (gold) surface (see paragraph [0116], lines 5-11).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make a biotinylated thiol self-assembled monolayer on the metal surface as taught by Spinkle et al. to use as an electrochemical sensor as taught by Choong et al. One of ordinary skill in the art would have been motivated to make a biotinylated thiol self-assembled monolayer on the metal surface as taught by Spinkle et al. to use as an electrochemical sensor as taught by Choong et al. for the advantage of providing a surface with no nonspecific binding and high efficiency in specific binding between different components (Spinkle: pg. 1825, left col., lines 16-21). Although the self-assembled monolayer on the gold metal surface of Spinkle et al. is use in surface plasmon resonance, Wink et al. teach that a surface modified with sulfur containing self-assembled monolayer is employed in application such as electrochemical and surface plasmon resonance (Wink: pg. 45R, right col., line 1 thru pg. 48R, left col., line 2).

Thus, any a surface modified with sulfur containing self-assembled monolayer use for surface plasmon resonance sensor can also be use for electrochemical sensor. In addition, the instant specification on page 24, paragraph [0116], recite using the procedure of Spinkle et al. for depositing biotin-DAD-C12-SH (12-mercapto(8-biotinamide-3,6-dioxaoctyl)dodecanamide) onto an Au (gold) surface (see paragraph [0116], lines 5-11). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Spinkle et al. teach the success of binding HCG to the monoclonal antibody on the biotinylated gold surface (Spinkle: pg. 1824, right col., lines 22-39).

Therefore, the combine teachings of Choong et al., Spinkle et al., and Wink et al. do render the apparatus and method of the instant claims *prima facie* obvious.

13. Claims 84, 91, and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Spinkle et al. (*Langmuir*, **1993**, 9(7), pgs. 1821-1825) and Wink et al. (*The Analyst*, **1997**, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129 above, and further in view of Cozzette et al. (US Patent 5,200,051) alone or as evidenced by Heller et al. (US Patent 5,403,700) regarding chromium as another type of metal-substrate adhesive.

For ***claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129***, Choong et al., Spinkle et al., and Wink et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129.

The combine teachings of Choong et al., Spinkle et al., and Wink et al. differs from the presently claimed invention as follows:

For ***claims 84, 91, and 92***, the combine teachings of Choong et al., Spinkle et al., and Wink et al. differ from the claimed invention by not reciting the use of an adhesive underneath each of the electrodes wherein the adhesive is chromium.

However, the combine teachings of Cozzette et al. and Heller et al. teach the limitations that are deficient in the combine teachings of Choong et al., Spinkle et al., and Wink et al.

For ***claims 84, 91, and 92***, Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the biosensor comprises a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). Although Cozzette et al. disclose titanium as a metal-substrate adhesive, other type of metal-substrate adhesive are known such as chromium as evidence by Heller et al. wherein the adhesive layer include compounds such as chromium or titanium (col. 6, lines 54-68 to col. 7, lines 1-4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use of an adhesive underneath each of the electrodes wherein the adhesive

is chromium as taught by Cozzette et al. and Heller et al. in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. One of ordinary skill in the art would have been motivated to use of an adhesive underneath each of the electrodes wherein the adhesive is chromium as taught by Cozzette et al. and Heller et al. in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. for the advantage of providing an adhesive layer that promotes the adhesion of the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-61). Moreover, both Choong et al. and Cozzette et al. disclose a biosensor comprising three-electrode system, i.e. analogous art (Choong: col. 5, lines 37-44; Cozzette: col. 12, lines 26-44). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Spinkle et al., Wink et al., Cozzette et al. and Heller et al. because Cozzette et al. teach several successful examples of using a chromium adhesive underneath each of the electrodes of the electrochemical sensor (Cozzette: col. 68, line 40 thru col. 69, line 63).

Therefore, the combine teachings of Choong et al., Spinkle et al., Wink et al., Cozzette et al. and Heller et al. do render the apparatus and method of the instant claims *prima facie* obvious.

14. Claims 93, 102, 121, and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Spinkle et al. (*Langmuir*, **1993**, 9(7), pgs. 1821-1825) and Wink et al. (*The Analyst*, **1997**, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129 above, and further in view of Weetall (US Patent 4,963,245).

For ***claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129***, Choong et al., Spinkle et al., and Wink et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129.

The combine teachings of Choong et al., Spinkle et al., and Wink et al. differs from the presently claimed invention as follows:

For ***claim 93***, the combine teachings of Choong et al., Spinkle et al., and Wink et al. differ from the claimed invention by not reciting that the substrate includes a well structure containing at least one of the electrodes.

For ***claims 102, 121, and 122***, the combine teachings of Choong et al., Spinkle et al., and Wink et al. differ from the claimed invention by not reciting that a) the reference electrode and the counter electrode each have a shape that is different from a shape of the working electrode; b) the reference electrode is arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode; and c) the counter electrode is arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode.

However, Weetall teaches the limitations that are deficient in the combine teachings of Choong et al., Spinkle et al., and Wink et al.

For ***claims 93, 102, 121, and 122***, Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-

68; claim 1). The sensor apparatus comprises a planar support with a plurality of wells (refers to the instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode; and an ammeter to control and monitor the electrodes in the wells/sampling area (see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) is at the perimeter of the working electrode (refers to the instant claims 102, 121, and 122).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make a) substrate with a well structure containing at least one of the electrode; b) the reference electrode and the counter electrode each have a shape that is different from a shape of the working electrode; c) the reference electrode is arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode; and d) the counter electrode is arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode as taught by Weetall in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. One of ordinary skill in the art would have been motivated to make a) substrate with a well structure containing at least one of the electrode; b) the reference electrode and the counter electrode each have a shape that is different from a shape of the working electrode; c) the reference electrode is arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode; and d) the counter electrode is

arranged about the perimeter of the working electrode such that a portion of the working electrode is positioned between different regions of the reference electrode as taught by Weetall in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. because the shape and arrangement of the substrate and electrodes would be a choice of experimental design and is considered within the purview of the cited prior art. Moreover, both Choong et al. and Weetall teaches a biosensor comprising three-electrode system, i.e. analogous art (Choong: col. 5, lines 37-44; Weetall: col. 1, lines 56-62). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Spinkle et al., Wink et al., and Weetall because Weetall disclose by example the success of the apparatus that include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122.

Therefore, the combine teachings of Choong et al., Spinkle et al., Wink et al., and Weetall do render the apparatus and method of the instant claims *prima facie* obvious.

15. Claim 95 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Spinkle et al. (*Langmuir*, **1993**, 9(7), pgs. 1821-1825) and Wink et al. (*The Analyst*, **1997**, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129 above, and further in view of Han et al. (US Patent 6,268,161 B1).

For ***claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129***, Choong et al., Spinkle et al., and Wink et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection

above (incorporated in its entirety herein by reference), which renders obvious claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129.

The combine teachings of Choong et al., Spinkle et al., and Wink et al. differs from the presently claimed invention as follows:

For ***claim 95***, the combine teachings of Choong et al., Spinkle et al., and Wink et al. differ from the claimed invention by not reciting the calibration step that uses two different calibration solutions.

However, Han et al. teaches the limitations that are deficient in the combine teachings of Choong et al., Spinkle et al., and Wink et al.

For ***claim 95***, Han et al. disclosed a biosensor for measuring the concentration of organic molecules in a solution (see e.g. col. 1, lines 16-17). Han et al. claim a method of using the biosensor that included a calibration step (see e.g. col. 12, lines 33-35; col. 16, claim 20). The claim method step includes a control solution (calibration solution) and obtaining a signal. Additionally, the system can be recalibrated by using a calibration solution with unknown amount of analyte (see e.g. col. 12, lines 60-62).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the calibration step that uses two different calibration solutions as taught by Han et al. in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. One of ordinary skill in the art would have been motivated to include the calibration step that uses two different calibration solutions in the electrochemical sensor of the combine teachings of Choong et al., Spinkle et al., and Wink et al. for the advantage of determining the performance of the electrode before the analysis of the sample

(Han: col. 12, lines 34-36). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Spinkle et al., Wink et al., and Han et al. because the calibration step is necessary to ensuring the working order of the electrode.

Therefore, the combine teachings of Choong et al., Spinkle et al., Wink et al., and Han et al. do render the apparatus and method of the instant claims *prima facie* obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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